CBER / CDER Consolidation

8th Annual GMP by the Sea
Cambridge, MD

August 26, 2003

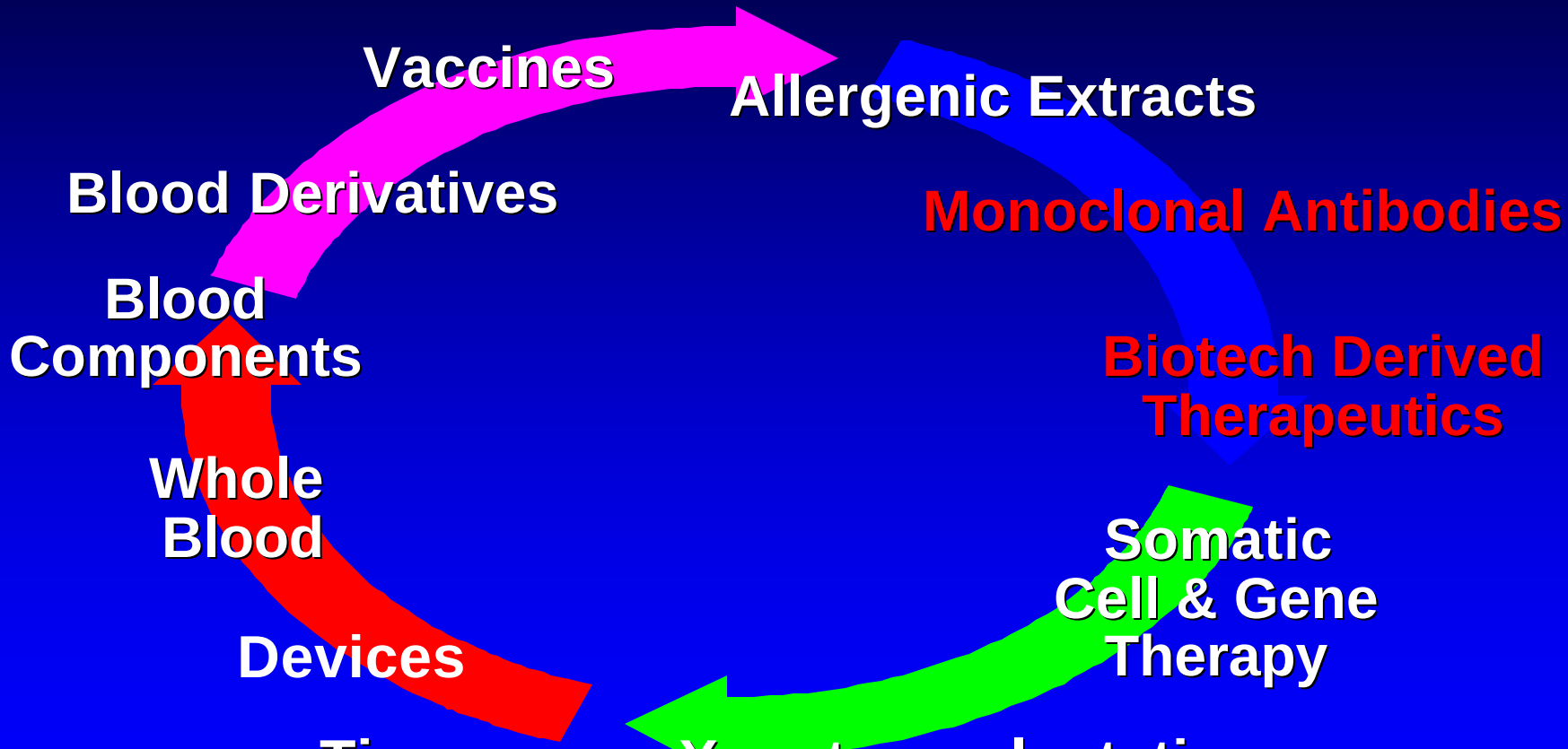
Mark A. Elengold

Deputy Director, Operations

Center For Biologics Evaluation and Research

Food and Drug Administration

BIOLOGICAL PRODUCTS REGULATED BY CBER



The OTRR, CBER record

- **Science-based regulation of biologic therapeutics at OTRR has played a central role in the development and availability of safe and effective products of biotechnology that are revolutionizing medicine.**
- **OTRR scientists/physicians work independently of but closely with regulated biotechnology.**
  - **Extraordinary number of meetings**
  - **Timely, science based guidance**
- **OTRR scientists/physicians have provided international leadership in the science-based regulation of biotechnology products.**

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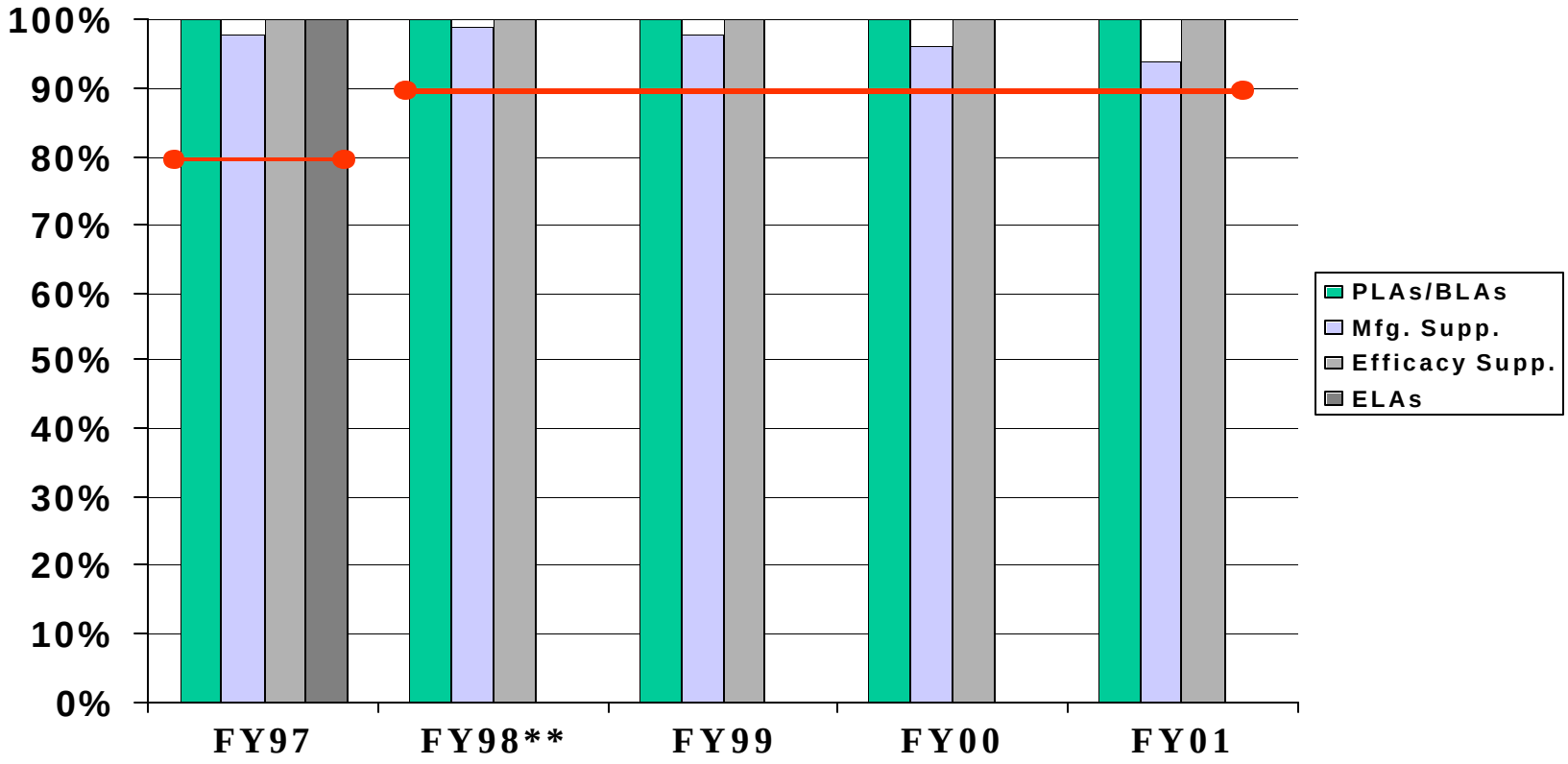
The OTRR, CBER record (continued)

- **The number of new product approvals is increasing.**
- **Despite the complexity and novelty of biotechnology products, review times and approval times compare favorably with those for other types of drugs.**
- **Biological therapeutics are often available first in the U.S.**
- **There has *never* been need to recall an OTRR-approved biotechnology drug due to safety concerns.**

CBER Biologics License Application Approvals for Biotechnology Products 1981-2002

Years	Therapeutics*	Vaccines	IVD	Total
1981-85	0	0	23	23
1986-90	6	2	35	43
1991-95	13	0	59	72
1996-00	26	2	26	54
2000-02	11	2	5	18
Total	56	6	148	210

CBER User Fee Review Performance
License Applications and Supplements
% of First Actions Within Goal*
By Cohort Fiscal Years 1997-2001



* PDUFA Performance Goals: FY97 - FY01=90% (Indicated by Red Lines)
** Beginning in FY98 ELAs were no longer included in PDUFA goals

(253bp)RIMS 12/26/02

CBER PDUFA II Procedural and Processing Goals Performance (as of December 31, 2002)

Regulatory Meetings Management											
			Actions Within Goal			Actions Overdue				
Fiscal Year	Goal	Meeting Requests Received	Completed	Pending	Total	Completed	Pending	Total	% Completed Within Goal[1]	*PDUFA Goal*
FY 1999	Response	387	283	0	283	104	0	104	73%	*70%*
	Held	364	321	0	321	43	0	43	88%	
	Minutes	328	282	0	282	46	0	46	86%	
FY 2000	Response	312	302	0	302	10	0	10	97%	*80%*
	Held	294	277	0	277	14	3	17	94%	
	Minutes	251	229	0	229	19	3	22	91%	
FY 2001	Response	388	379	0	379	9	0	9	98%	*90%*
	Held	341	330	0	330	10	1	11	97%	
	Minutes	293	286	0	286	7	0	7	98%	
FY 2002	Response	415	401	0	401	12	2	14	97%	*90%*
	Held	374	360	0	360	9	5	14	96%	
	Minutes	335	317	2	319	6	10	16	95%	

[1] - of those that have reached the goal date

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CBER PDUFA II Procedural and Processing Goals Performance – *cont.*
(as of December 31, 2002)

Special Protocol Assessment

Fiscal Year	Protocol Review Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	0								60%
FY 2000	0								70%
FY 2001	1	1	0	1	0	0	0	100%	80%
FY 2002	4	4	0	4	0	0	0	100%	90%

Major Dispute Resolution

Fiscal Year	Dispute Resolution Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	1	1	0	1	0	0	0	100%	70%
FY 2000	0								80%
FY 2001	2	2	0	2	0	0	0	100%	90%
FY 2002	4	4	0	4	0	0	0	100%	90%

Responses to Clinical Holds

Fiscal Year	Responses to Clinical Holds Received	Actions Within Goal			Actions Overdue			% Completed Within Goal[1]	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1998	22	18	0	18	4	0	4	82%	75%
FY 1999	77	73	0	73	4	0	4	95%	90%
FY 2000	89	87	0	87	2	0	2	98%	90%
FY 2001	125	115	0	115	10	0	10	92%	90%
FY 2002	121	118	0	119	3	0	3	98%	90%

[1] - of those that have reached the goal date

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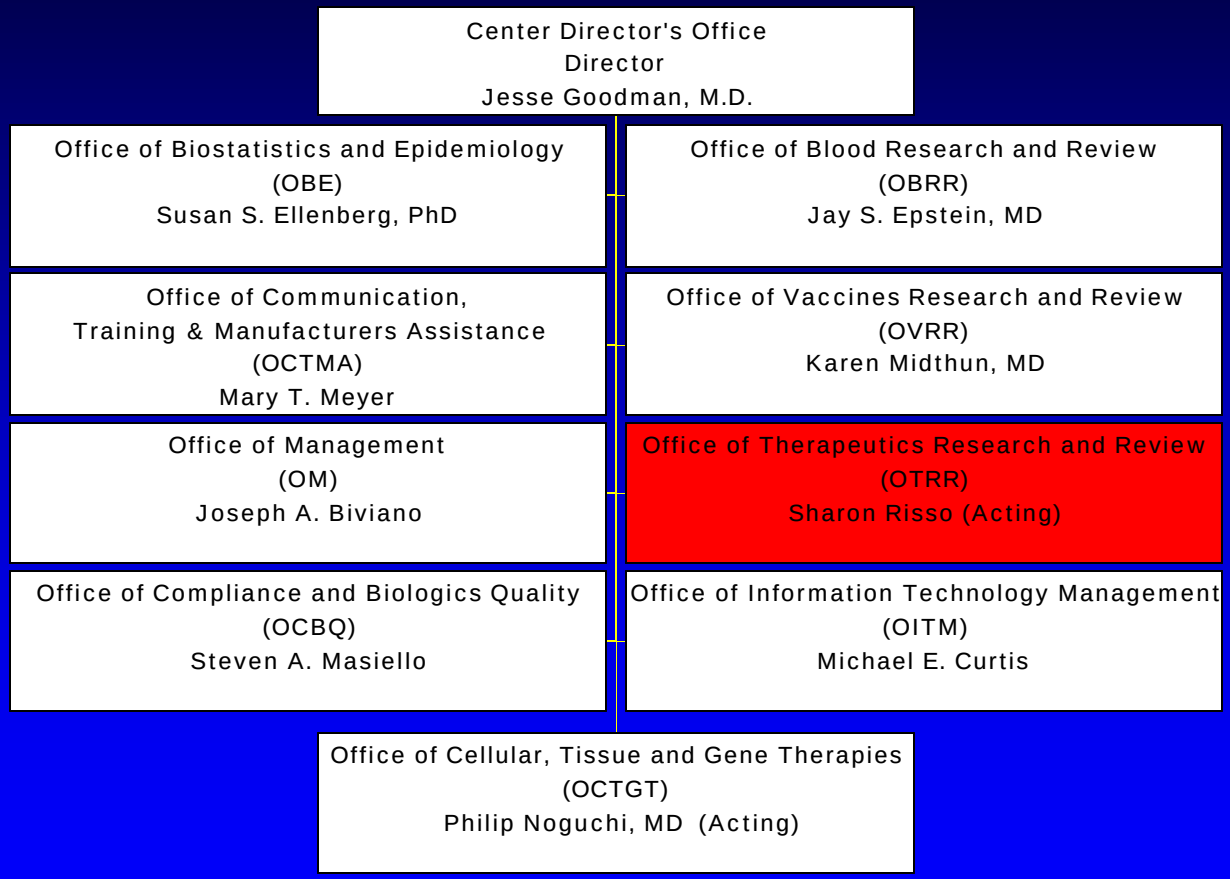
CBER Review Performance
FY 2002 Cohort of User Fee Applications

Application Types	Numbers				Percent of Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
New Products	10	9	0	1	22%	0%
Effectiveness Supplements	11	11	2	0	45%	0%
Manufacturing Supplements	748	748	378	0	74%	1%

AP=Approved, RTF=Refuse To file, UN=Unacceptable For Filing, WF=Withdrawn Before Filing

CBER Organization



What Went

- **Monoclonal antibodies**
- **Cytokines, growth factors, enzymes, interferons -- (including recombinant versions)**
- **Proteins intended for therapeutic use that are extracted from animals or microorganisms (except clotting factors**
- **Other therapeutic immunotherapies**

What Stayed

- Monoclonal antibodies, cytokines, growth factors, or other proteins when used solely as an ex vivo constituent in a manufacturing process / when used solely as a reagent in the production of a product that is under the jurisdiction of CBER
- Viral-vectored gene insertions (i.e., “gene therapy”)
- Products composed of human or animal cells or from physical parts of those cells

What Stayed (continued)

- Plasma expanders
- Allergen patch tests
- Allergenics
- Antitoxins, antivenins, and venoms
- In vitro diagnostics
- Vaccines
- Toxoids and toxins intended for immunization

CBER

The People

Office	FTEs	Bodies	Total
OD	0	2	2
OM	1	1	2
OCTMA	2	1	3
OBE	6	6	12
OIM	0	2	2
OCBQ	2	16	18
OTRR		161	161
Buy-Back	8	0	8
PDUFA	8	0	8
TOTAL	**27**	**189**	**216**

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The Products

PRODUCT	CBER	CDER
IND	1748	1162
IDE	163	1
BLA (approved)	1259	59
BLA (pending)	36	9
NDA (approved)	60	3
NDA (pending)	1	0
PMA (approved)	18	0
PMA (pending)	3	0
510k (approved)	671	0
510k (pending)	26	0
ANDA (approved)	8	0

Timeline

- **June 20**
  - Letter to Sponsors
  - Transfer Web Site
- **June 30**
  - Transfer of Regulatory Responsibility
  - Detail of OTRR and other personnel to CDER
- **October 1**
  - Transfer of personnel
  - Reprogramming of resources

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Notification Letter

- To all Sponsors
- Warns that Regulatory Responsibility Will Shift for Certain products
- Identifies Product Categories
- Directs Sponsors to Lists of Specific Files on CBER Web Site

Notification Letter (cont.)

- In most cases, the Regulatory Project Manager and assigned reviewers will not change since many of these staff will be reassigned to CDER
- Directs Sponsors to Continue Addressing submissions for Transferred Products to the CBER Document Control Center until further notice
- Address Questions to CBER's Office of Communication, Training and Manufacturers Assistance

Web Site

- **http://www.fda.gov/cber/transfer/transfer.htm**
- **Links**
  - **Notification Letter**
  - **List of Approved Products Transferring to CDER**
  - **Lists of Products Transferring and Remaining, Organized by File Type and Tracking Number**

Transfer of Therapeutic Products to the Center for Drug Evaluation and Research

Sponsor Letter

June 20, 2003

Dear Sponsor,

As you may know, the regulatory responsibility, review and continuing oversight, for many biologic therapeutic products will be transferred from the Center for Biologics Evaluation and Research (CBER) to the Center for Drug Evaluation and Research (CDER). This change in regulatory responsibility will result in the transfer of your IND, IDE, BLA, or NDA if it belongs to one of the following product classes:

- Monoclonal antibodies for in-vivo use
- Cytokines, growth factors, enzymes, immunomodulators, and thrombolytics
- Proteins intended for therapeutic use that are extracted from animals or microorganisms, including recombinant versions of these products (except clotting factors)
- Other non-vaccine therapeutic immunotherapies

The following product classes will remain at CBER:

- Vaccines (e.g., "gene therapy")
- Products composed of human or animal cells or from physical parts of these cells
- Allergenic products
- Allergenics
- Antitoxins, antivenins, and venoms
- In vitro diagnostics
- Vaccines, including therapeutic vaccines
- Toxoids and toxins intended for immunization
- Blood, blood components and related products

Products that are used solely as an ex vivo constituent in a manufacturing process for a biologic (e.g., protein to activate somatic cells) should be described in the IND for the investigational product (e.g., somatic cells) or in a drug master file submitted in support of the IND.

To determine which Center will be working on your files, we have posted lists of products remaining and being transferred. You may access these lists, which are organized by file type and tracking number at http://www.fda.gov/cber/transfer/transfer.htm. Questions about file assignment should be directed to CBER's Office of Communication, Training and Manufacturers Assistance by telephone 800-835-4709, 301-827-1800, fax 301-827-3843, or email to MAT@cber.fda.gov.

For those products being transferred, the change in review responsibility will be effective June 30, 2003. In most cases, the Regulatory Project Manager and assigned reviewers will not change since many of these staff will be reassigned to CDER. For the time being, all applications and correspondence, including adverse event reports and biological product deviation reports, should continue to be addressed to the CBER Document Control Center until further notice. The correct mailing address for all files is as follows: CBER Document Control Center (HFM-99), 1401 Rockville Pike, Suite 200N, Rockville, Maryland 20852-1448.

If your file is being transferred to CDER, you will be advised of any changes in procedures when they occur.

We hope that the goals of this product transfer initiative will benefit our stakeholders and we look forward to a successful transition to this new alignment.

— signature —

Jesse L. Goodman, M.D., M.P.H.
Director
Center for Biologics Evaluation and Research

— signature —

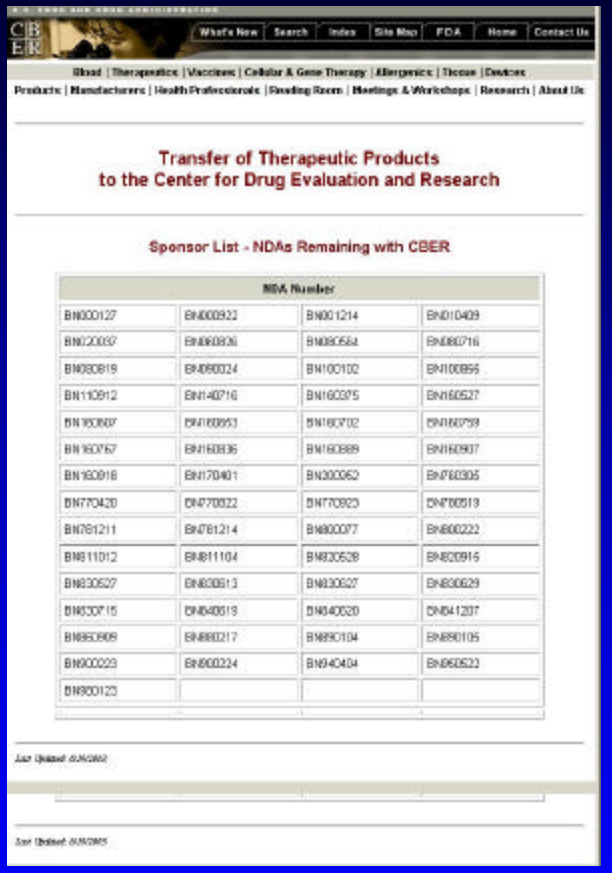
Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

Last Updated: 6/20/03

Transfer of Therapeutic Products to the Center for Drug Evaluation and Research

Approved Products Transferring to CDER

Last Updated: 6/20/03

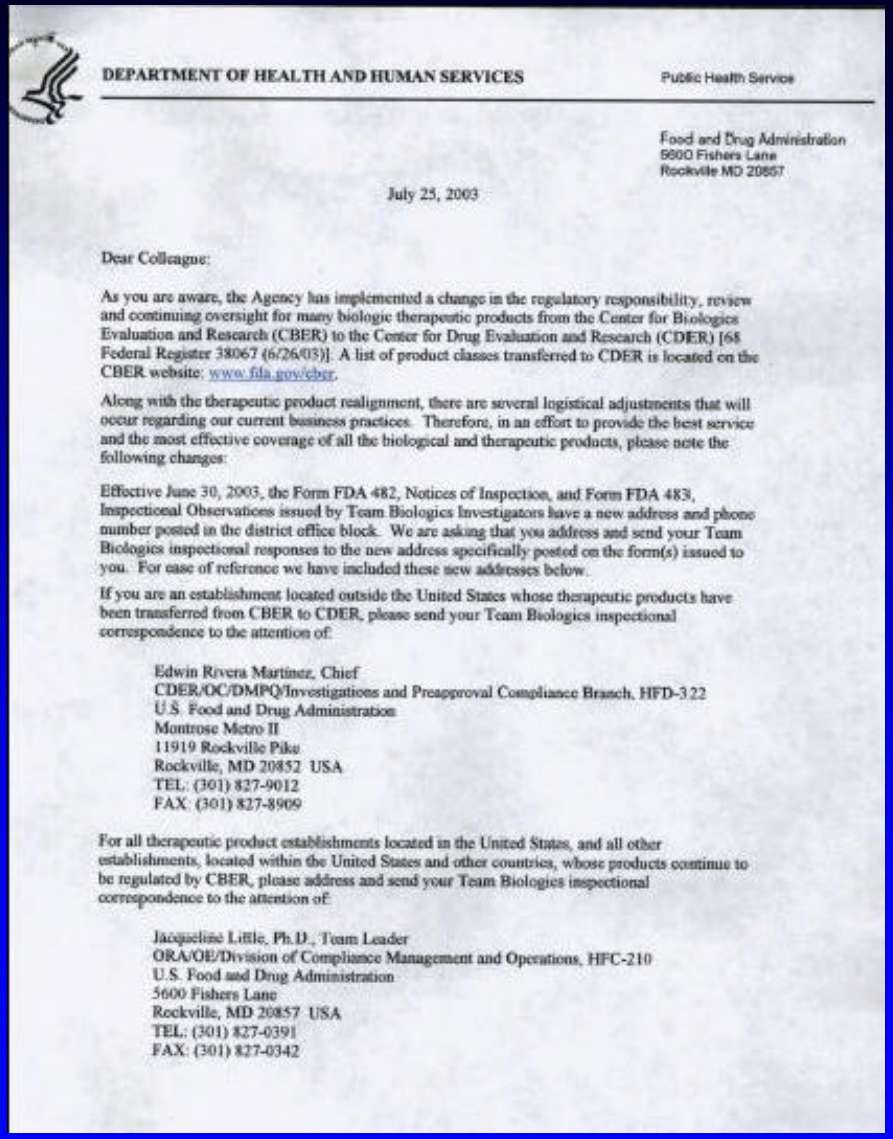


Transfer of Therapeutic Products to the Center for Drug Evaluation and Research

Sponsor List - NDAs Remaining with CBER

NDA Number			
BN000127	BN000922	BN001214	BN010409
BN020037	BN060826	BN080564	BN080716
BN080819	BN080824	BN100102	BN100866
BN110912	BN140716	BN160375	BN160527
BN160697	BN160853	BN160702	BN160758
BN160767	BN160836	BN160889	BN160907
BN160918	BN170401	BN200062	BN760305
BN770420	BN770822	BN770823	BN780513
BN781211	BN781214	BN800077	BN800222
BN811012	BN811104	BN820528	BN820916
BN830527	BN830613	BN830627	BN830629
BN830715	BN840519	BN840520	BN841207
BN860909	BN880217	BN890104	BN890105
BN900029	BN900224	BN940404	BN960523
BN900123			

Last Updated: 6/6/2005



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857

July 25, 2003

Dear Colleague:

As you are aware, the Agency has implemented a change in the regulatory responsibility, review and continuing oversight for many biologic therapeutic products from the Center for Biologics Evaluation and Research (CBER) to the Center for Drug Evaluation and Research (CDER) [68 Federal Register 38067 (6/26/03)]. A list of product classes transferred to CDER is located on the CBER website: www.fda.gov/cber.

Along with the therapeutic product realignment, there are several logistical adjustments that will occur regarding our current business practices. Therefore, in an effort to provide the best service and the most effective coverage of all the biological and therapeutic products, please note the following changes:

Effective June 30, 2003, the Form FDA 482, Notices of Inspection, and Form FDA 483, Inspectional Observations issued by Team Biologics Investigators have a new address and phone number posted in the district office block. We are asking that you address and send your Team Biologics inspectional responses to the new address specifically posted on the form(s) issued to you. For ease of reference we have included these new addresses below.

If you are an establishment located outside the United States whose therapeutic products have been transferred from CBER to CDER, please send your Team Biologics inspectional correspondence to the attention of:

Edwin Rivera Martinez, Chief
CDER/OC/DMPQ/Investigations and Preapproval Compliance Branch, HFD-322
U.S. Food and Drug Administration
Montrose Metro II
11919 Rockville Pike
Rockville, MD 20852 USA
TEL: (301) 827-9012
FAX: (301) 827-8909

For all therapeutic product establishments located in the United States, and all other establishments, located within the United States and other countries, whose products continue to be regulated by CBER, please address and send your Team Biologics inspectional correspondence to the attention of:

Jacqueline Little, Ph.D., Team Leader
ORA/OE/Division of Compliance Management and Operations, HFC-210
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857 USA
TEL: (301) 827-0391
FAX: (301) 827-0342

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Finally, to enhance our ability to perform a timely review, we are asking you to voluntarily forward additional copies of your response to the Team Biologics Investigators at the addresses they provide, and if you are an establishment involved in the manufacture of biological products that remain under the purview of CBER, please provide a copy of your response to CBER OCBQ/Division of Inspections and Surveillance, HFM-650, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448 USA.

Through this ongoing transition, we strive to continually provide excellent customer service to you. Questions regarding the contents of this letter should be directed to Mr. Rivera Martinez or Dr. Little, at the addresses and/or phone numbers listed above.

Sincerely yours,

Donald Vasbinder, Acting

Director
Office of Enforcement
Office of Regulatory Affairs

CBER

We're Here to Help You!

WWW.FDA.GOV/CBER

- **Email CBER:**
  - **Manufacturers: matt@cber.fda.gov**
  - **Consumers, health care professionals: octma@cber.fda.gov**
- **Phone:**
  - **800-835-4709**
  - **301-827-1800**